APPENDIX A–1 STEPWISE APPROACH FOR MANAGING ASTHMA

Figure 1. Stepwise Approach for Managing Infants and Young Children (5 Years of Age and Younger) With Acute or Chronic Asthma (Updates EPR-2 Figures 3–4a and 3–6)

Classify Severity: Clinical Features Before Treatment or Adequate Control	Symptoms/Day Symptoms/Night	Medications Required To Maintain Long-Term Control Daily Medications
Step 4 Severe Persistent	Continual Frequent	■ Preferred treatment: – High-dose inhaled corticosteroids AND – Long-acting inhaled beta$_2$-agonists AND, if needed, – Corticosteroid tablets or syrup long term (2 mg/kg/day, generally do not exceed 60 mg per day). (Make repeat attempts to reduce systemic corticosteroids and maintain control with high-dose inhaled corticosteroids.)
Step 3 Moderate Persistent	Daily >1 night/week	■ Preferred treatments: – Low-dose inhaled corticosteroids and long-acting inhaled beta$_2$-agonists OR – Medium-dose inhaled corticosteroids. ■ Alternative treatment: – Low-dose inhaled corticosteroids and either leukotriene receptor antagonist or theophylline. If needed (particularly in patients with recurring severe exacerbations): ■ Preferred treatment: – Medium-dose inhaled corticosteroids and long-acting beta$_2$-agonists. ■ Alternative treatment: – Medium-dose inhaled corticosteroids and either leukotriene receptor antagonist or theophylline.
Step 2 Mild Persistent	>2/week but <1x/day >2 nights/month	■ Preferred treatment: – Low-dose inhaled corticosteroids (with nebulizer or MDI with holding chamber with or without face mask or DPI). ■ Alternative treatment (listed alphabetically): – Cromolyn (nebulizer is preferred or MDI with holding chamber) OR leukotriene receptor antagonist.
Step 1 Mild Intermittent	≤2 days/week ≤2 nights/month	■ No daily medication needed.

Quick Relief
All Patients

- Bronchodilator as needed for symptoms. Intensity of treatment will depend upon severity of exacerbation.
  - Preferred treatment: **Short-acting inhaled beta$_2$-agonists** by nebulizer or face mask and space/holding chamber
  - Alternative treatment: Oral beta$_2$-agonists
- With viral respiratory infection
  - Bronchodilator q 4–6 hours up to 24 hours (longer with physician consult); in general, repeat no more than once every 6 weeks
  - Consider systemic corticosteroid if exacerbation is severe or patient has history of previous severe exacerbations
- Use of short-acting beta$_2$-agonists >2 times a week in intermittent asthma (daily, or increasing use in persistent asthma) may indicate the need to initiate (increase) long-term-control therapy.

Step down
Review treatment every 1 to 6 months; a gradual stepwise reduction in treatment may be possible.

Step up
If control is not maintained, consider step up. First, review patient medication technique, adherence, and environmental control.

Goals of Therapy: Asthma Control

- Minimal or no chronic symptoms day or night
- Minimal or no exacerbations
- No limitations on activities; no school/parent's work missed
- Minimal use of short-acting inhaled beta$_2$-agonist
- Minimal or no adverse effects from medications

Note

- The stepwise approach is intended to assist, not replace, the clinical decisionmaking required to meet individual patient needs.
- Classify severity: assign patient to most severe step in which any feature occurs.
- There are very few studies on asthma therapy for infants.
- Gain control as quickly as possible (a course of short systemic corticosteroids may be required); then step down to the least medication necessary to maintain control.
- Minimize use of short-acting inhaled beta$_2$-agonists. Over-reliance on short-acting inhaled beta$_2$-agonists (e.g., use of short-acting inhaled beta$_2$-agonist every day, increasing use or lack of expected effect, or use of approximately one canister a month even if not using it every day) indicates inadequate control of asthma and the need to initiate or intensify long-term-control therapy.
- Provide parent education on asthma management and controlling environmental factors that make asthma worse (e.g., allergies and irritants).
- Consultation with an asthma specialist is recommended for patients with moderate or severe persistent asthma. Consider consultation for patients with mild persistent asthma.

APPENDIX A–1. STEPWISE APPROACH FOR MANAGING ASTHMA (continued)

Figure 2. Stepwise Approach for Managing Asthma in Adults and Children Older Than 5 Years of Age: Treatment (Updates EPR-2 Figures 3–4a and 3–4b)

Classify Severity: Clinical Features Before Treatment or Adequate Control	Symptoms/Day Symptoms/Night	PEF or FEV_1 PEF Variability	Medications Required To Maintain Long-Term Control Daily Medications
Step 4 Severe Persistent	Continual Frequent	≤60% >30%	■ Preferred treatment: – High-dose inhaled corticosteroids AND – Long-acting inhaled $beta_2$-agonists AND, if needed, – Corticosteroid tablets or syrup long term (2 mg/kg/day, generally do not exceed 60 mg per day). (Make repeat attempts to reduce systemic corticosteroids and maintain control with high-dose inhaled corticosteroids.)
Step 3 Moderate Persistent	Daily >1 night/week	>60% – <80% >30%	■ Preferred treatment: – Low-to-medium dose inhaled corticosteroids and long-acting inhaled $beta_2$-agonists. ■ Alternative treatment (listed alphabetically): – Increase inhaled corticosteroids within medium-dose range OR – Low-to-medium dose inhaled corticosteroids and either leukotriene modifier or theophylline. If needed (particularly in patients with recurring severe exacerbations): ■ Preferred treatment: – Increase inhaled corticosteroids within medium-dose range and add long-acting inhaled $beta_2$-agonists. ■ Alternative treatment: – Increase inhaled corticosteroids within medium-dose range and add either leukotriene modifier or theophylline.
Step 2 Mild Persistent	>2/week but < 1x/day >2 nights/month	≥80% 20–30%	■ Preferred treatment: – Low-dose inhaled corticosteroids. ■ Alternative treatment (listed alphabetically): cromolyn, leukotriene modifier, nedocromil, OR sustained release theophylline to serum concentration of 5–15 mcg/mL.
Step 1 Mild Intermittent	≤2 days/week ≤2 nights/month	≥80% <20%	■ No daily medication needed. ■ Severe exacerbations may occur, separated by long periods of normal lung function and no symptoms. A course of systemic corticosteroids is recommended.

Quick Relief
All Patients

- Short-acting bronchodilator: 2–4 puffs **short-acting inhaled $beta_2$-agonists** as needed for symptoms.
- Intensity of treatment will depend on severity of exacerbation; up to 3 treatments at 20-minute intervals or a single nebulizer treatment as needed. Course of systemic corticosteroids may be needed.
- Use of short-acting $beta_2$-agonists >2 times a week in intermittent asthma (daily, or increasing use in persistent asthma) may indicate the need to initiate (increase) long-term-control therapy.

Step down
Review treatment every 1 to 6 months; a gradual stepwise reduction in treatment may be possible.

Step up
If control is not maintained, consider step up. First, review patient medication technique, adherence, and environmental control.

Goals of Therapy: Asthma Control

- Minimal or no chronic symptoms day or night
- Minimal or no exacerbations
- No limitations on activities; no school/work missed
- Maintain (near) normal pulmonary function
- Minimal use of short-acting inhaled $beta_2$-agonist
- Minimal or no adverse effects from medications

Note

- The stepwise approach is meant to assist, not replace, the clinical decisionmaking required to meet individual patient needs.
- Classify severity: assign patient to most severe step in which any feature occurs (PEF is % of personal best; FEV_1 is % predicted).
- Gain control as quickly as possible (consider a short course of systemic corticosteroids); then step down to the least medication necessary to maintain control.
- Minimize use of short-acting inhaled $beta_2$-agonists. Over-reliance on short-acting inhaled $beta_2$-agonists (e.g., use of short-acting inhaled $beta_2$-agonist every day, increasing use or lack of expected effect, or use of approximately one canister a month even if not using it every day) indicates inadequate control of asthma and the need to initiate or intensify long-term-control therapy.
- Provide education on self-management and controlling environmental factors that make asthma worse (e.g., allergens and irritants).
- Refer to an asthma specialist if there are difficulties controlling asthma or if step 4 care is required. Referral may be considered if step 3 care is required.

APPENDIX A–2. USUAL DOSAGES FOR ASTHMA MEDICATIONS

Figure 1. Usual Dosages for Long-Term-Control Medications (Updates EPR-2 Figure 3–5a)

Medication	Dosage Form	Adult Dose	Child Dose*	Comments
Inhaled Corticosteroids *(See Estimated Comparative Daily Dosages for Inhaled Corticosteroids.)*				
Systemic Corticosteroids			(Applies to all three corticosteroids)	
Methylprednisolone	2, 4, 8, 16, 32 mg tablets	■ 7.5–60 mg daily in a single dose in a.m. or qod as needed for control	■ 0.25–2 mg/kg daily in single dose in a.m. or qod as needed for control	■ For long-term treatment of severe persistent asthma, administer single dose in a.m. either daily or on alternate days (alternate-day therapy may produce less adrenal suppression). If daily doses are required, one study suggests improved efficiency and no increase in adrenal suppression when administered at 3 p.m. (Beam et al. 1992).
Prednisolone	5 mg tablets, 5 mg/5 cc, 15 mg/5 cc	■ Short-course "burst": to achieve control 40–60 mg per day as single or 2 divided doses for 3–10 days	■ Short-course "burst": 1–2 mg/kg/day, maximum 60 mg/day for 3–10 days	■ Short courses or "bursts" are effective for establishing control when initiating therapy or during a period of gradual deterioration.
Prednisone	1, 2.5, 5, 10, 20, 50 mg tablets; 5 mg/cc, 5 mg/5 cc			■ The burst should be continued until patient achieves 80% PEF personal best or symptoms resolve. This usually requires 3–10 days but may require longer. There is no evidence that tapering the dose following improvement prevents relapse.
Long-Acting Inhaled Beta$_2$-Agonists				■ **Should not be used for symptom relief or exacerbations. Use with corticosteroids.**
Salmeterol	MDI 21 mcg/puff	2 puffs q 12 hours	1–2 puffs q 12 hours	■ May use one dose nightly for symptoms.
	DPI 50 mcg/blister	1 blister q 12 hours	1 blister q 12 hours	
Formoterol	DPI 12 mcg/single-use capsule	1 capsule q 12 hours	1 capsule q 12 hours	■ Efficacy and safety have not been studied in children <5 years of age. ■ Each capsule is for single use only; additional doses should not be administered for at least 12 hours. ■ Capsules should be used only with the Aerolizor™ inhaler and should not be taken orally.

APPENDIX A–2. USUAL DOSAGES FOR ASTHMA MEDICATIONS (continued)

Figure 1. Usual Dosages for Long-Term-Control Medications (Updates EPR-2 Figure 3–5a)

Medication	Dosage Form	Adult Dose	Child Dose*	Comments
Combined Medication				
Fluticasone/Salmeterol	DPI 100 mcg, 250 mcg, or 500 mcg/ 50 mcg	1 inhalation bid; dose depends on severity of asthma	1 inhalation bid; dose depends on severity of asthma	■ Not FDA approved in children <12 years of age. 100/50 for patient not controlled on low-to-medium dose inhaled corticosteroids. 250/50 for patients not controlled on medium-to-high dose inhaled corticosteroids.
Cromolyn and Nedocromil				
Cromolyn	MDI 1 mg/puff Nebulizer 20 mg/ampule	2–4 puffs tid-qid 1 ampule tid-qid	1–2 puffs tid-qid 1 ampule tid-qid	■ One dose prior to exercise or allergen exposure provides effective prophylaxis for 1–2 hours.
Nedocromil	MDI 1.75 mg/puff	2–4 puffs bid-qid	1–2 puffs bid-qid	■ See cromolyn above.
Leukotriene Modifiers				
Montelukast	4 mg or 5 mg chewable tablet 10 mg tablet	10 mg qhs	■ 4 mg qhs (2–5 years of age) 5 mg qhs (6–14 years of age) 10 mg qhs (>14 years of age)	■ Montelukast exhibits a flat dose-response curve. Doses >10 mg will not produce a greater response in adults.
Zafirlukast	10 or 20 mg tablet	40 mg daily (20 mg tablet bid)	■ 20 mg daily (7–11 years of age) (10 mg tablet bid)	■ For zafirlukast, administration with meals decreases bioavailability; take at least 1 hour before or 2 hours after meals.
Zileuton	300 or 600 mg tablet	2,400 mg daily (give tablets qid)		■ For zileuton, monitor hepatic enzymes (ALT).
Methylxanthines				
Theophylline	Liquids, sustained-release tablets, and capsules	Starting dose 10 mg/kg/day up to 300 mg max; usual max 800 mg/day	Starting dose 10 mg/kg/day; usual max: ■ <1 year of age: 0.2 (age in weeks) + 5 = mg/kg/day ■ ≥1 year of age: 16 mg/kg/day	■ Adjust dosage to achieve serum concentration of 5–15 mcg/mL at steady-state (at least 48 hours on same dosage). ■ Due to wide interpatient variability in theophylline metabolic clearance, **routine serum theophylline level monitoring is important.** ■ See figure 3–5a, page 87, EPR-2 for factors that can affect theophylline levels.

* Children ≤12 years of age

APPENDIX A–2. USUAL DOSAGES FOR ASTHMA MEDICATIONS (continued)

Figure 2. Estimated Comparative Daily Dosages for Inhaled Corticosteroids (Updates EPR-2 Figure 3–5b)

Drug	Low Daily Dose		Medium Daily Dose		High Daily Dose	
	Adult	Child*	Adult	Child*	Adult	Child*
Beclomethasone CFC 42 or 84 mcg/puff	168–504 mcg	84–336 mcg	504–840 mcg	336–672 mcg	>840 mcg	>672 mcg
Beclomethasone HFA 40 or 80 mcg/puff	80–240 mcg	80–160 mcg	240–480 mcg	160–320 mcg	>480 mcg	>320 mcg
Budesonide DPI 200 mcg/inhalation	200–600 mcg	200–400 mcg	600–1,200 mcg	400–800 mcg	>1,200 mcg	>800 mcg
Inhalation suspension for nebulization (child dose)		0.5 mg		1.0 mg		2.0 mg
Flunisolide 250 mcg/puff	500–1,000 mcg	500–750 mcg	1,000–2,000 mcg	1,000–1,250 mcg	>2,000 mcg	>1,250 mcg
Fluticasone MDI: 44, 110, or 220 mcg/puff	88–264 mcg	88–176 mcg	264–660 mcg	176–440 mcg	>660 mcg	>440 mcg
DPI: 50, 100, or 250 mcg/inhalation	100–300 mcg	100–200 mcg	300–600 mcg	200–400 mcg	>600 mcg	>400 mcg
Triamcinolone acetonide 100 mcg/puff	400–1,000 mcg	400–800 mcg	1,000–2,000 mcg	800–1,200 mcg	>2,000 mcg	>1,200 mcg

* Children ≤12 years of age

Note

- **The most important determinant of appropriate closing is the clinician's judgment of the patient's response to therapy.** The clinician must monitor the patient's response on several clinical parameters and adjust the dose accordingly. The stepwise approach to therapy emphasizes that once control of asthma is achieved, the dose of medication should be carefully titrated to the minimum dose required to maintain control, thus reducing the potential for adverse effect.
- Comparative dosages in the EPR-2 were based on a limited number of published comparative clinical trials and extrapolation of differences in topical potency and lung delivery. This updated comparative dosage chart is based on review of recently published clinical trials involving more than 5,000 patients and published reviews (Barnes PJ et al. 1998; Kelly 1998; Pedersen 1997). The key differences from the EPR-2 include a higher dosage of budesonide and recommendations for two newly available medications: beclomethasone HFA and budesonide suspension for nebulization. The rationale for these changes is summarized as follows:
  - The high dose is the dose that appears likely to be the threshold beyond which significant hypothalamic-pituitary-adrenal (HPA) axis suppression is produced, and, by extrapolation, the risk is increased for other clinically significant systemic effects if used for prolonged periods of time (Martin et al. 2002; Szefler et al. 2002).
  - The low and medium dose reflects findings from dose-ranging studies in which incremental efficacy within the low-to-medium dose ranges was established without increased systemic effect as measured by overnight cortisol excretion. The studies demonstrated a relatively flat dose-response curve for efficacy at the medium-dose range; that is, increasing the dose to high-dose range did not significantly increase efficacy but did increase systemic effect (Martin et al. 2002; Szefler et al. 2002).
  - The dose for budesonide dry powder inhaler (DPI) is based on recently available comparative data with other medications, rather than the comparison to budesonide metered-dose inhaler (MDI) that was used in the EPR-2. These new data, including a meta-analysis of seven studies, show that budesonide DPI is comparable to approximately one-half the microgram dose of fluticasone (Barnes NC et al. 1998; Nielsen and Dahl 2000).
  - The dose for beclomethasone HFA is one-half the dose for beclomethasone CFC, based on studies demonstrating that the different pharmaceutical properties of the medications result in enhanced lung delivery for the HFA (a less forceful spray from the HFA propellant and a reengineered nozzle that allows a smaller particle size) (Leach et al. 1998; Busse et al. 1999; Gross et al. 1999; Thompson et al. 1998).
  - The dose for budesonide nebulizer suspension is based on efficacy and safety studies (Baker et al. 1999; Kemp et al. 1999; Shapiro et al. 1998), but no comparative studies with other inhaled corticosteroids are available. It is noted that the efficacy studies did not demonstrate a clear or consistent dose-response, although the high dose of 2.0 mg was effective in a placebo-controlled study in 40 infants with severe asthma (de Blic et al. 1996). In a small open-label long-term safety study, the ACTH stimulated cortisols appeared lower in the 13 infants receiving the high dose of 2.0 mg budesonide compared to infants receiving lower doses, but this was not statistically significant due, perhaps, to the small study size (Scott and Skoner 1999).
- Some doses may be outside package labeling, especially in the high dose range.
- MDI dosages are expressed as the actuater dose (the amount of the drug leaving the actuater and delivered to the patient), which is the labeling required in the United States. This is different from the dosage expressed as the valve dose (the amount of drug leaving the valve, all of which is not available to the patient), which is used in many European countries and in some scientific literature. DPI doses are expressed as the amount of drug in the inhaler following activation.

APPENDIX A–2. USUAL DOSAGES FOR ASTHMA MEDICATIONS (continued)

Figure 3. Usual Dosages for Quick-Relief Medications (Updates EPR-2 Figure 3–5d)

Medication	Dosage Form	Adult Dose	Child Dose*	Comments
Short-Acting Inhaled Beta$_2$-Agonists				
	MDI			
Albuterol Albuterol HFA Pirbuterol	90 mcg/puff, 200 puffs 90 mcg/puff, 200 puffs 200 mcg/puff, 400 puffs	■ 2 puffs 5 minutes prior to exercise ■ 2 puffs tid-qid prn	■ 1–2 puffs 5 minutes prior to exercise ■ 2 puffs tid-qid prn	■ An increasing use or lack of expected effect indicates diminished control of asthma. ■ Not generally recommended for long-term treatment. Regular use on a daily basis indicates the need for additional long-term-control therapy. ■ Differences in potency exist but all products are essentially comparable on a per puff basis. ■ May double usual dose for mild exacerbations. ■ Nonselective agents (i.e., epinephrine, isoproterenol, metaproterenol) are not recommended due to their potential for excessive cardiac stimulation, especially in high doses.
	DPI			
Albuterol Rotahaler	200 mcg/capsule	1–2 capsules q 4–6 hours as needed and prior to exercise	1 capsule q 4–6 hours as needed and prior to exercise	
	Nebulizer solution			
Albuterol	5 mg/mL (0.5%) 2.5 mg/mL 1.25 mg/3 mL 0.63 mg/3 mL	1.25–5 mg in 3 cc of saline q 4–8 hours	0.05 mg/kg (min 1.25 mg, max 2.5 mg) in 3 cc of saline q 4–6 hours	May mix with cromolyn or ipratropium nebulizer solutions. May double dose for severe exacerbations.
	Nebulizer solution			
Bitolterol	2 mg/mL (0.2%)	0.5–3.5 mg (0.25–1 cc) in 2–3 cc of saline q 4–8 hours	Not established	May not mix with other nebulizer solutions.
	Nebulizer solution			
Levalbuterol (R-albuterol)	0.31 mg/3 mL 0.63 mg/3 mL 1.25 mg/3 mL	0.63 mg–2.5 mg q 4–8 hours	0.025 mg/kg (min. 0.63 mg, max. 1.25 mg) q 4–8 hours	0.63 mg of levalbuterol is equivalent in efficacy and side effects to 1.25 mg of racemic albuterol. The product is a sterile-filled preservative-free unit dose vial.

APPENDIX A–2. USUAL DOSAGES FOR ASTHMA MEDICATIONS (continued)

Figure 3. Usual Dosages for Quick-Relief Medications (Updates EPR-2 Figure 3–5d)

Medication	Dosage Form	Adult Dose	Child Dose*	Comments
Anticholinergics				
	MDI			
Ipratropium	18 mcg/puff, 200 puffs	2–3 puffs q 6 hours	1–2 puffs q 6 hours	Evidence is lacking for anticholinergics producing added benefit to beta$_2$-agonists in long-term-control asthma therapy.
	Nebulizer solution			
	0.25 mg/mL (0.025%)	0.25 mg q 6 hours	0.25–0.5 mg q 6 hours	
	MDI			
Ipratropium with albuterol	18 mcg/puff of ipratropium bromide and 90 mcg/puff of albuterol.	2–3 puffs q 6 hours	1–2 puffs q 8 hours	
	200 puffs/canister			
	Nebulizer solution			
	0.5 mg/3 mL ipratropium bromide and 2.5 mg/3 mL albuterol	3 mL q 4–6 hours	1.5–3 mL q 8 hours	Contains EDTA to prevent discoloration of the solution. This additive does not induce bronchospasm.
Systemic Corticosteroids			(Applies to the first three corticosteroids)	
Methylprednisolone	2, 4, 6, 8, 16, 32 mg tablets	■ Short course "burst": 40–60 mg/day as single or 2 divided doses for 3–10 days	■ Short course "burst" 1–2 mg/kg/day, maximum 60 mg/day, for 3–10 days	■ Short courses or "bursts" are effective for establishing control when initiating therapy or during a period of gradual deterioration. ■ The burst should be continued until patient achieves 80% PEF personal best or symptoms resolve. This usually requires 3–10 days but may require longer. There is no evidence that tapering the dose following improvement prevents relapse.
Prednisolone	5 mg tablets, 5 mg/5 cc, 15 mg/5 cc			
Prednisone	1, 2.5, 5, 10, 20, 50 mg tablets; 5 mg/cc, 5 mg/5 cc			
	Repository injection			
(Methylprednisolone acetate)	40 mg/mL 80 mg/mL	240 mg IM once	7.5 mg/kg IM once	May be used in place of a short burst of oral steroids in patients who are vomiting or if adherence is a problem.

*Children ≤12 years of age

APPENDIX A–2. USUAL DOSAGES FOR ASTHMA MEDICATIONS

Figure 4. Dosages of Drugs for Asthma Exacerbations in Emergency Medical Care or Hospital (Updates EPR-2 Figure 3–10)

	Dosages		
Medication	**Adult Dose**	**Child Dose***	**Comments**
Short-Acting Inhaled $Beta_2$-Agonists			
Albuterol			
Nebulizer solution (5.0 mg/mL, 2.5 mg/3 mL, 1.25 mg/3 mL, 0.63 mg/3 mL)	2.5–5 mg every 20 minutes for 3 doses, then 2.5–10 mg every 1–4 hours as needed, or 10–15 mg/hour continuously	0.15 mg/kg (minimum dose 2.5 mg) every 20 minutes for 3 doses, then 0.15–0.3 mg/kg up to 10 mg every 1–4 hours as needed, or 0.5 mg/kg/hour by continuous nebulization	Only selective $beta_2$-agonists are recommended. For optimal delivery, dilute aerosols to minimum of 3 mL at gas flow of 6–8 L/min.
MDI (90 mcg/puff)	4–8 puffs every 20 minutes up to 4 hours, then every 1–4 hours as needed	4–8 puffs every 20 minutes for 3 doses, then every 1–4 hours inhalation maneuver. Use spacer/holding chamber	As effective as nebulized therapy if patient is able to coordinate.
Bitolterol			
Nebulizer solution (2 mg/mL)	See albuterol dose	See albuterol dose; thought to be half as potent as albuterol on a mg basis	Has not been studied in severe asthma exacerbations. Do not mix with other drugs.
MDI (370 mcg/puff)	See albuterol dose	See albuterol dose	Has not been studied in severe asthma exacerbations.
Levalbuterol (R-albuterol)			
Nebulizer solution (0.63 mg/3 mL, 1.25 mg/3 mL)	1.25–2.5 mg every 20 minutes for 3 doses, then 1.25–5 mg every 1–4 hours as needed, or 5–7.5 mg/hour continuously	0.075 mg/kg (minimum dose 1.25 mg) every 20 minutes for 3 doses, then 0.075–0.15 mg/kg up to 5 mg every 1–4 hours as needed, or 0.25 mg/kg/hour by continuous nebulization	0.63 mg of levalbuterol is equivalent to 1.25 mg of racemic albuterol for both efficacy and side effects.
Pirbuterol			
MDI (200 mcg/puff)	See albuterol dose	See albuterol dose; thought to be half as potent as albuterol on a mg basis	Has not been studied in severe asthma exacerbations.
Systemic (Injected) $Beta_2$-Agonists			
Epinephrine 1:1000 (1 mg/mL)	0.3–0.5 mg every 20 minutes for 3 doses sq	0.01 mg/kg up to 0.3–0.5 mg every 20 minutes for 3 doses sq	No proven advantage of systemic therapy over aerosol.
Terbutaline (1 mg/mL)	0.25 mg every 20 minutes for 3 doses sq	0.01 mg/kg every 20 minutes for 3 doses then every 2–6 hours as needed sq	No proven advantage of systemic therapy over aerosol.

APPENDIX A–2. USUAL DOSAGES FOR ASTHMA MEDICATIONS (continued)

Figure 4. Dosages of Drugs for Asthma Exacerbations in Emergency Medical Care or Hospital (Updates EPR-2 Figure 3–10)

	Dosages		
Medication	**Adult Dose**	**Child Dose***	**Comments**
Anticholinergics			
Ipratropium bromide			
Nebulizer solution (0.25 mg/mL)	0.5 mg every 30 minutes for 3 doses then every 2–4 hours as needed	0.25 mg every 20 minutes for 3 doses, then every 2 to 4 hours	May mix in same nebulizer with albuterol. Should not be used as first-line therapy; should be added to beta$_2$-agonist therapy.
MDI (18 mcg/puff)	4–8 puffs as needed	4–8 puffs as needed	Dose delivered from MDI is low and has not been studied in asthma exacerbations.
Ipratropium with albuterol			
Nebulizer solution (each 3 mL vial contains 0.5 mg ipratropium bromide and 2.5 mg albuterol)	3 mL every 30 minutes for 3 doses, then every 2–4 hours as needed	1.5 mL every 20 minutes for 3 doses, then every 2–4 hours	Contains EDTA to prevent discoloration. This additive does not induce bronchospasm.
MDI (each puff contains 18 mcg ipratropium bromide and 90 mcg of albuterol)	4–8 puffs as needed	4–8 puffs as needed	
Systemic Corticosteroids		(Applies to the first three corticosteroids)	
Prednisone **Methylprednisolone** **Prednisolone**	120–180 mg/day in 3 or 4 divided doses for 48 hours, then 60–80 mg/day until PEF reaches 70% of predicted or personal best	1 mg/kg every 6 hours for 48 hours then 1–2 mg/kg/day (maximum = 60 mg/day) in 2 divided doses until PEF 70% of predicted or personal best	For outpatient "burst" use 40–60 mg in single or 2 divided doses for adults (children: 1–2 mg/kg/day, maximum 60 mg/day) for 3–10 days.

*Children ≤12 years of age

Note

No advantage has been found for higher dose corticosteroids in severe asthma exacerbations, nor is there any advantage for intravenous administration over oral therapy provided gastrointestinal transit time or absorption is not impaired. The usual regimen is to continue the frequent multiple daily dose until the patient achieves an FEV_1 or PEF of 50 percent of predicted or personal best and then lower the dose to twice daily. This usually occurs within 48 hours. Therapy following a hospitalization or emergency department visit may last from 3 to 10 days. If patients are then started on inhaled corticosteroids, studies indicate there is no need to taper the systemic corticosteroid dose. If the followup systemic corticosteroid therapy is to be given once daily, one study indicates that it may be more clinically effective to give the dose in the afternoon at 3 p.m., with no increase in adrenal suppression (Beam et al. 1992).

REFERENCES (APPENDIX A-2, FIGURES 1 AND 2)

Baker JW, Mellon M, Wald J, Welch M, Cruz-Rivera M, Walton-Bowen K. A multiple-dosing, placebo-controlled study of budesonide inhalation suspension given once or twice daily for treatment of persistent asthma in young children and infants. *Pediatrics* 1999;102(2):414–21.

Barnes NC, Hallett C, Harris TA. Clinical experience with fluticasone propionate in asthma: a meta-analysis of efficacy and systemic activity compared with budesonide and beclomethasone dipropionate at half the microgram dose or less. *Respir Med* 1998;92(1):95–104.

Barnes PJ, Pedersen S, Busse WW. Efficacy and safety of inhaled corticosteroids. New developments. Am J Respir Crit Care Med 1998;157(suppl):S1-S53.

Beam WR, Weiner DE, Martin RJ. Timing of prednisone and alterations or airways inflammation in nocturnal asthma. *Am Rev Respir Dis* 1992; 146(6):1524–30.

Busse WW, Brazinsky S, Jacobson K, Stricker W, Schmitt K, Vanden Burgt J, Donnell D, Hannon S, Colice GL et al. Efficacy response of inhaled beclomethasone dipropionate in asthma is proportional to dose and is improved by formulation with a new propellant. *J Allergy Clin Immunol* 1999;104(6):1215–22

de Blic J, Delacourt C, Le Bourgeois M, Mahut B, Ostinelli J, Caswell C, Scheinmann P. Efficacy of nebulized budesonide in treatment of severe infantile asthma: a double-blind study. *J Allergy Clin Immunol* 1996;98(1):14–20.

Gross G, Thompson PJ, Chervinsky P, Vanden Burgt J. Hydrofluoroalkane-134a beclomethasone dipropionate, 400 µg, is as effective as chlorofluorocarbon beclomethasone dipropionate, 800 µg, for the treatment of moderate asthma. *Chest* 1999;115(2):343–51.

Kelly HW. Comparison of inhaled corticosteroids. *Ann Pharmacother* 1998;32(2):220–32.

Kemp JP, Skoner D, Szefler SJ, Walton-Bowen K, Cruz-Rivera M, Smith JA. Once-daily budesonide inhalation suspension for the treatment of persistent asthma in infants and young children. *Ann Allergy Asthma Immunol* 1999;83(3):231–9.

Leach CL, Davidson PJ, Boudreau RJ. Improved airway targeting with the CFC-free HFA-beclomethasone metered-dose inhaler compared with CFC-beclomethasone. *Eur Respir J* 1998;12(6):1346–53.

Martin RJ, Szefler SJ, Chinchilli VM, Kraft M, Dolovich M, Boushey HA, Cherniack RM, Craig TJ, Drazen JM, Fagan JK et al. Systemic effect comparisons of six inhaled corticosteroid preparations. *Am J Respir Crit Care Med* 2002;165:1377–83.

National Heart, Lung, and Blood Institute, National Asthma Education and Prevention Program. *Guidelines for the diagnosis and management of asthma.* Expert Panel Report 2, Publication No. 97-4051. Bethesda, MD: U.S. Department of Health and Human Services; 1997.

Nielsen LP, Dahl R. Therapeutic ratio of inhaled corticosteroids in adult asthma: A dose-range comparison between fluticasone propionate and budesonide, measuring their effect on bronchial hyperresponsiveness and adrenal cortex function. *Am J Respir Crit Care Med* 2000;162(6): 2053–7.

Pedersen S, O'Byrne P. A comparison of the efficacy and safety of inhaled corticosteroids in asthma. *Allergy* 1997;52(39 suppl):1–34.

Scott MB, Skoner DP. Short-term and long-term safety of budesonide inhalation suspension in infants and young children with persistent asthma. *J Allergy Clin Immunol* 1999;104:(4 Pt 2)200–9.

Shapiro G, Mendelson L, Kraemer MJ, Cruz-Rivera M, Walton-Bowen K, Smith JA. Efficacy and safety of budesonide inhalation suspension (Pulmicort Respules) in young children with inhaled steroid-dependent, persistent asthma. *J Allergy Clin Immunol* 1998;102(5):789–96.

Szefler SJ, Martin RJ, King TS, Boushey HA, Cherniack RM, Chinchilli VM, Craig TJ, Dolovich M, Drazen JM, Fagan JK, et al. Significant variability in response to inhaled corticosteroids for persistent asthma. *J Allergy Clin Immunol* 2002;109(3):410–8.

Thompson PJ, Davies RJ, Young WF, Grossman AB, Donnell D. Safety of hydrofluoroalkane-134a beclomethasone dipropionate extrafine aerosol. *Respir Med* 1998;92(suppl):33–39.